

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C. 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

| | |
|---|---|
| Date of mailing (day/month/year) 05 May 2000 (05.05.00) | |
| International application No. PCT/GB99/03013 | Applicant's or agent's file reference 23576 |
| International filing date (day/month/year) 10 September 1999 (10.09.99) | Priority date (day/month/year) 11 September 1998 (11.09.98) |
| Applicant OLIVER, Roy, Frederick et al | |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

11 April 2000 (11.04.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

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| <p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p> | <p>Authorized officer Juan Cruz</p> <p>Telephone No.: (41-22) 338.83.38</p> |
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| | | |
|--|---|---|
| Applicant's or agent's file reference 23576 | <div style="display: flex; justify-content: space-between;"> <div style="text-align: center;"> FOR FURTHER ACTION </div> <div style="font-size: small;"> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. </div> </div> | |
| International application No. PCT/GB 99/ 03013 | International filing date (day/month/year) <div style="text-align: center;">10/09/1999</div> | (Earliest) Priority Date (day/month/year) <div style="text-align: center;">11/09/1998</div> |
| Applicant TISSUE SCIENCE LABORATORIES LIMITED et al. | | |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the International search was carried out on the basis of the International application in the language in which it was filed, unless otherwise indicated under this item.

☐ the International search was carried out on the basis of a translation of the International application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the International application, the International search was carried out on the basis of the sequence listing :

☐ contained in the International application in written form.

☐ filed together with the International application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the International application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/GB 99/03013

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61L27/36 A61L27/26

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | EP 0 251 695 A (COLLAGEN CORP) 7 January 1988 (1988-01-07) claims; examples 1-4 | 1-9 |
| X | US 5 256 140 A (FALLICK HARRY) 26 October 1993 (1993-10-26) claims | 1-9 |
| X | US 4 582 640 A (SMESTAD THOMAS L ET AL) 15 April 1986 (1986-04-15) claims | 1-9 |
| X | US 4 837 285 A (BERG RICHARD A ET AL) 6 June 1989 (1989-06-06) claims; examples | 1-9 |
| | -/- | |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"Z" document member of the same patent family

Date of the actual completion of the international search

10 December 1999

Date of mailing of the international search report

20/12/1999

Name and mailing address of the ISA

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Authorized officer

ESPINOSA, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/03013

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| X | WO 93 13755 A (COLETICA) 22 July 1993 (1993-07-22) claims | 1-9 |
| A | EP 0 697 218 A (COLLAGEN CORP) 21 February 1996 (1996-02-21) claims; examples 1-10 | 1-9 |
| A | EP 0 083 868 A (COLLAGEN CORP) 20 July 1983 (1983-07-20) claims | 1-9 |
| A | US 5 523 291 A (JANZEN ERNST ET AL) 4 June 1996 (1996-06-04) cited in the application claims; example | 1-9 |
| A | US 5 705 488 A (JANZEN ERNST ET AL) 6 January 1998 (1998-01-06) cited in the application claims | 1-9 |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/03013

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
|---|---|---------------------|----------------------------|---------------------|
| EP 0251695 | A | 07-01-1988 | US 4803075 A | 07-02-1989 |
| | | | AU 7467187 A | 07-01-1988 |
| | | | JP 1899011 C | 23-01-1995 |
| | | | JP 6022581 B | 30-03-1994 |
| | | | JP 63119772 A | 24-05-1988 |
| US 5256140 | A | 26-10-1993 | NONE | |
| US 4582640 | A | 15-04-1986 | AT 27821 T | 15-07-1987 |
| | | | CA 1224210 A | 14-07-1987 |
| | | | EP 0089145 A | 21-09-1983 |
| | | | JP 1036840 B | 02-08-1989 |
| | | | JP 1554411 C | 23-04-1990 |
| | | | JP 58170796 A | 07-10-1983 |
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| | | | AU 4210585 A | 01-11-1985 |
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| | | | ES 541629 A | 01-04-1986 |
| | | | FI 854692 A | 27-11-1985 |
| | | | IT 1182725 B | 05-10-1987 |
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| | | | JP 61502129 T | 25-09-1986 |
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| | | | WO 8504413 A | 10-10-1985 |
| | | | US 4841962 A | 27-06-1989 |
| | | | US 4925924 A | 15-05-1990 |
| | | | US 4937323 A | 26-06-1990 |
| | | | US 4703108 A | 27-10-1990 |
| WO 9313755 | A | 22-07-1993 | FR 2686250 A | 23-07-1993 |
| | | | AT 136773 T | 15-05-1996 |
| | | | DE 69302262 D | 23-05-1996 |
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| | | | EP 0621776 A | 02-11-1994 |
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| | | | JP 7503001 T | 30-03-1995 |
| | | | US 5658593 A | 19-08-1997 |
| EP 0697218 | A | 21-02-1996 | US 5550187 A | 27-08-1996 |
| | | | US 5643464 A | 01-07-1997 |
| | | | US 5527856 A | 18-06-1997 |
| EP 0083868 | A | 20-07-1983 | US 4424208 A | 03-01-1984 |
| | | | CA 1199580 A | 21-01-1986 |
| | | | JP 1329859 C | 30-07-1986 |
| | | | JP 58121958 A | 20-07-1983 |
| | | | JP 60054288 B | 29-11-1985 |
| US 5523291 | A | 04-06-1996 | AU 675879 B | 20-02-1997 |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/03013

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|---|--|
| US 5523291 A | | AU 7685794 A BR 9407420 A CA 2170754 A CN 1133562 A EP 0717634 A JP 9502372 T WO 9507095 A US 5705488 A | 27-03-1995 12-11-1996 16-03-1995 16-10-1996 26-06-1996 11-03-1997 16-03-1995 06-01-1998 |
| US 5705488 A | 06-01-1998 | US 5523291 A AU 675879 B AU 7685794 A BR 9407420 A CA 2170754 A CN 1133562 A EP 0717634 A JP 9502372 T WO 9507095 A | 04-06-1996 20-02-1997 27-03-1995 12-11-1996 16-03-1995 16-10-1996 26-06-1996 11-03-1997 16-03-1995 |

REC'D 27 DEC 2000

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| | | |
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| Applicant's or agent's file reference 23576 | | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) FOR FURTHER ACTION |
| International application No. PCT/GB99/03013 | International filing date (day/month/year) 10/09/1999 | Priority date (day/month/year) 11/09/1998 |
| International Patent Classification (IPC) or national classification and IPC A61L27/36 | | |
| Applicant TISSUE SCIENCE LABORATORIES LIMITED et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

| | |
|---|--|
| Date of submission of the demand 11/04/2000 | Date of completion of this report 21.12.2000 |
| Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Authorized officer Bochelen, D Telephone No. +49 89 2399 8150  |

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/03013

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

Description, pages:

1-12 as originally filed

Claims, No.:

1-8 with telefax of 26/09/2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/03013

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|-------------------------------|------|--------|----------|
| Novelty (N) | Yes: | Claims | 4 |
| | No: | Claims | 1-3, 5-8 |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-8 |
| Industrial applicability (IA) | Yes: | Claims | 1-8 |
| | No: | Claims | |

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/03013

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1) Reference is made to the following documents:

- D1: EP-A-0 251 695 (COLLAGEN CORP) 7 January 1988 (1988-01-07)
- D2: US-A-5 256 140 (FALLICK HARRY) 26 October 1993 (1993-10-26)
- D3: US-A-4 582 640 (SMESTAD THOMAS L ET AL) 15 April 1986 (1986-04-15)
- D4: US-A-4 837 285 (BERG RICHARD A ET AL) 6 June 1989 (1989-06-06)
- D5: WO 93 13755 A (COLETICA) 22 July 1993 (1993-07-22)
- D6: EP-A-0 083 868 (COLLAGEN CORP) 20 July 1983 (1983-07-20)
- D7: US-A-5 523 291 (JANZEN ERNST ET AL) 4 June 1996 (1996-06-04) cited in the application
- D8: US-A-5 705 488 (JANZEN ERNST ET AL) 6 January 1998 (1998-01-06) cited in the application

2) **Novelty (Art. 33 (1) and (2) PCT):**

Claims 1-3, 5-8 appear to be not new. The prior art discloses compositions suitable for implants comprising particles of collagen (D1: p2 l49 and p3 l32; D2: col2 l3; D3: claim 1; D4: col2 l23; D5: p5 l13; D6: p2 l13), free of foreign material (D4: col3 l15) the collagen being cross-linked (D1: p3 l33; D3: col6 l8; D4: col3 l17; D5: p6 l25; D6: p2 l13) dispersed in biocompatible medium (D1: p3 l9; D2: col3 l11; D3: col6 l8; D4: col4 l48, claim 8; D5: p5 l16, claim 1; D6: p6 l13) that is saline (D1: p3 l39; D2: p3 l3; D3: claim 1; D4: col5 l22; D6: p6 l28), a dextran solution (D1: p8 table2; D5: p6 l3), glycerol (D1: p8 table2; D4: col5 l18;) or a polysaccharide (D1: p8 table2; D5: p5 l14). The particle size (D3: col10 l33; D4: col 3 l23; D5: p7 l29-31; D6: p6 l8), concentration of solids (D1: claim 4; D5: p7 l36) and consistency (D4: col8 l38) of the compositions fall within the scope of claims 6, 7 and 8.

The technical feature of claim 1 contemplating collagenous particles sufficiently large to preserve the original architecture of the natural tissue is not clear enough

to delimit claim 1 from the prior art. Even, when the specific particle size of dependent claim 6 are taken into account, the subject-matter of the claims is not delimited from the prior art.

Claim 4 appears to be new. The prior art discloses implant compositions containing collagenous material and elastin (D7: claim 1; D8: claim 1) from which said claim differs that the collagenous material is in form of particles.

3) Inventive step (Art. 33 (1) and (3) PCT):

Documents D7 and D8 describe compositions containing fibrillar collagen, eventually cross-linked (D7: col2 l65), and elastin (D7: col1 l36; D8: col1 l38). The starting material is an elastin rich ligament that is used to produce fibers of collagen and elastin after being milled. It would be obvious for a skilled person to prepare a composition according to claim 4 by adapting the method disclosed in D7 and D8. Therefore, the subject-matter of claim 4 does not involve an inventive step.

Re Item VII

Certain defects in the international application

- a) Costar (p10 l25) is a registered trademark but is not acknowledged as such.

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CLAIMS

1. An implant composition which comprises a biocompatible carrier medium having dispersed therein
5 particles of collagenous material where the particles are sufficiently large to preserve the original architecture and molecular structure of the natural tissue material from which they are derived and wherein the collagenous material is substantially free of non-
10 fibrous tissue proteins, glycoproteins, cellular elements and lipids or lipid residues and which is non-cytotoxic.
2. A composition according to Claim 1 wherein the
15 collagenous material is free or substantially free of antigenic polysaccharides and mucopolysaccharides.
3. A composition according to Claim 1 or 2 wherein the biocompatible medium is saline, dextran solution, or
20 glycerol or a non-toxic antigenic viscous polysaccharide.
4. A composition according to any one of Claims 1 to 3 wherein the collagenous material contains a proportion
25 of elastin.
5. A composition according to any one of Claims 1 to 4 wherein the collagenous material is cross-linked.
- 30 6. A composition according to any one of Claims 1 to 5 wherein the particle size of the particles of collagenous material is within the range of 50 to 500 microns.
- 35 7. A composition according to any one of the preceding Claims wherein the concentration of solids is 10 to 70 percent by weight and the consistency of the composition

- 14 -

is such as to enable it to administered by injection.

8. A composition according to any one of the preceeding
claims wherein the composition is of a pasty
5 consistency.